Message

From: Davis, Allen [Davis.Allen@epa.gov]
Sent: 12/17/2015 4:21:46 PM
To: Flowers, Lynn [Flowers.Lynn@epa.gov]; Vandenberg, John [Vandenberg.John@epa.gov]; D'Amico, Louis [DAmico.Louis@epa.gov]; Birchfield, Norman [Birchfield.Norman@epa.gov]; Ross, Mary [Ross.Mary@epa.gov]; Walsh, Debra [Walsh.Debra@epa.gov]; Cogliano, Vincent [cogliano.vincent@epa.gov]; Jones, Samantha [Jones.Samantha@epa.gov]; Olden, Kenneth [Olden.Kenneth@epa.gov]; Deener, Kathleen [Deener.Kathleen@epa.gov]
Subject: RE: Chloroprene summary -some points made by Sen Cassidy and relevant IRIS assessment and study files

Ex. 5 Deliberative Process (DP)

Hope this helps, let me know if you have any other questions.

J. Allen Davis, MSPH
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From: Flowers, Lynn
Sent: Thursday, December 17, 2015 11:13 AM
To: Vandenberg, John <Vandenberg.John@epa.gov>; D'Amico, Louis <DAmico.Louis@epa.gov>; Birchfield, Norman <Birchfield.Norman@epa.gov>; Ross, Mary <Ross.Mary@epa.gov>; Walsh, Debra <Walsh.Debra@epa.gov>; Davis, Allen <Davis.Allen@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>; Olden, Kenneth <Olden.Kenneth@epa.gov>; Deener, Kathleen <Deener.Kathleen@epa.gov>
Subject: RE: Chloroprene summary -some points made by Sen Cassidy and relevant IRIS assessment and study files

John: Thank you so much for sending this. Assuming that there will be more to do, it is good to have these summaries and papers in hand.

Ex. 5 Deliberative Process (DP)

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From: Vandenberg, John
Sent: Thursday, December 17, 2015 10:58 AM
To: D'Amico, Louis <DAmico.Louis@epa.gov>; Flowers, Lynn <Flowers.Lynn@epa.gov>; Birchfield, Norman <Birchfield.Norman@epa.gov>; Ross, Mary <Ross.Mary@epa.gov>; Walsh, Debra <Walsh.Debra@epa.gov>; Davis, Allen <Davis.Allen@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>; Olden, Kenneth <Olden.Kenneth@epa.gov>; Deener, Kathleen <Deener.Kathleen@epa.gov>
Subject: Chloroprene summary -some points made by Sen Cassidy and relevant IRIS assessment and study files
Importance: High

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

John

From: Davis, Allen
Sent: Thursday, December 17, 2015 9:00 AM
To: Vandenberg, John <Vandenberg.John@epa.gov>
Subject: Chloroprene files

John, see attached chloroprene files and links. I've also extracted out some text from the tox review that's pretty enlightening (in my opinion).

A number of occupational cohort studies have examined cancer mortality and incidence among workers exposed to chloroprene monomer and/or polychloroprene latex in the U.S., Russia (Moscow), Armenia, France, China, and Ireland (Bulbulyan et al., 1998, 625105; Bulbulyan et al., 1999, 157419; Colonna and Laydevant, 2001, 625112; Leet and Selevan, 1982, 094970; Li et al., 1989, 625181; Marsh et al., 2007, 625187; Marsh et al., 2007, 625188; Pell, 1978, 064957; Romazini et al., 1992, 624896). Concern that exposure to chloroprene may result in liver cancer derives principally from its structural similarity to vinyl chloride, a chemical known to cause liver angiosarcoma in humans.

Despite these differences in occupational exposure to chloroprene and other chemicals, four of the cohorts with observed liver/biliary passage cancer cases showed statistically significant associations (i.e., two- to fivefold increased risk) with chloroprene exposure. Four mortality studies (Table 4-11) reported SMRs of 339, 240, 482, 571 when compared to external populations (Bulbulyan et al., 1998, 625105; Bulbulyan et al., 1999, 157419; Leet and Selevan, 1982, 094970; Li et al., 1989, 625181).

The study involving four plants, including the Louisville Works plant included in the Leet and Selevan (1982, 094970) study by Marsh et al. (2007, 625188), which had the largest sample size and most extensive exposure assessment, also observed increased relative risk estimates for liver cancer in relation to cumulative exposure in the plant with the highest exposure levels (trend p-value = 0.09, RRs 1.0, 1.90, 5.10, and 3.33 across quartiles of exposure, based on 17 total cases). Although not statistically significant, these findings are consistent in magnitude with results (RR range: 2.9–7.1) detected in two other studies for high and intermediate cumulative exposures (Bulbulyan et al., 1998, 625105; Bulbulyan et al., 1999, 157419).

A key limitation of most of the chloroprene studies (and other occupational studies) is the potential for bias due to the healthy worker effect. Although this may be less of a concern for cancer mortality outcomes, SMR analyses are based on external comparisons to the general population and will often result in reduced SMR values for the occupational cohort. Two studies with more advanced chloroprene exposure assessment conducted internal analyses to reduce this source of bias (Bulbulyan et al., 1999, 157419; Marsh et al., 2007, 625188). Among these studies, only Bulbulyan et al. (1999, 157419) observed a statistically significant association between chloroprene exposure and liver cancer mortality.

With respect to liver cancer, the lack of data on alcohol consumption precluded its examination as a potential confounder, although there is no direct evidence that alcohol is related to the exposure of interest (i.e., chloroprene). Given the nature of the work environment for most of the study participants in these occupational studies, there is also the possibility of co-exposures which may be confounders, although Bulbulyan et al. (1999, 157419) discussed the known co-exposures at the study facility in Armenia and reported that none were known liver carcinogens. One study with data on a co-exposure (vinyl chloride) reported evidence of negative confounding (Marsh et al., 2007, 625188). This would result in an underestimate of the reported association between chloroprene and liver cancer if adjusted for vinyl chloride which suggests that this co-exposure was unlikely to explain the association observed between chloroprene and liver cancer in that population.

An additional paper by this group (Leonard et al., 2007, 625179) further explored the healthy worker effect in an analysis of the Louisville and Pontchartrain workers. Compared to the local county population estimates, SMRs were decreased for all cancers, respiratory cancers, and liver cancers. However, when comparisons were based on DuPont national and DuPont Region 1 comparison populations (in order to control for the healthy worker effect), the authors found statistically significant elevated risks for: all cancers, SMR = 111 (DuPont national population only); and respiratory cancer mortality, SMRs = 137 (DuPont national population) and 120 (DuPont Region 1 population). Elevated SMRs were observed for liver cancer, SMRs = 127 (DuPont national population) and 121 (DuPont Region 1 population), although these liver cancer risks were smaller than reported in other studies and were nonsignificant.

Link to NTP
report: http://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr400499/abstracts/tr467/index.html

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